

<b>Institution:</b> The University of Manchester		
<b>Unit of Assessment:</b> 3 (Allied Health Professions, Dentistry, Nursing and Pharmacy)		
<b>Title of case study:</b> Promoting oral health in medically compromised patients to improve patient outcomes		
<b>Period when the underpinning research was undertaken:</b> January 2006 - October 2017		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Anne-Marie Glenny	Professor of Health Sciences Reader in Evidence based healthcare Senior Lecturer in Evidence based healthcare	2013 - present 2012 - 2013 2008 - 2012
Helen Worthington	Professor of Evidence Based Care	2003 - present
Jan Clarkson	Professor of Clinical Effectiveness Honorary Professor	2013 - present 2010 - 2013
Philip Riley	Lecturer in Oral Health Research Fellow	2020 - present 2013 - 2020
Martin McCabe	Clinical Senior Lecturer	2009 - present
<b>Period when the claimed impact occurred:</b> August 2013 - July 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> N		
<b>1. Summary of the impact</b>		
<p>Maintaining good oral health is vital for general health and is particularly important for medically compromised patients. Cochrane Oral Health (COH) at the University of Manchester (UoM) identified, appraised and synthesised large, relevant bodies of evidence to:</p> <ul style="list-style-type: none"> <li>• identify interventions that minimise the negative impact of radiotherapy and chemotherapy on oral health and</li> <li>• reduce morbidity and mortality through the use of appropriate oral care measures to prevent ventilator-associated pneumonia (VAP) in critically ill patients.</li> </ul> <p>Our research findings have guided care provision internationally, leading to significant improvements in the oral care and management of disease in medically compromised patients. Through comprehensive synthesis of empirical evidence, we produced robust systematic reviews, previously lacking, to inform a series of national and international guidelines and influence decision-making.</p>		
<b>2. Underpinning research</b>		
<b>Prevention and treatment of oral conditions in patients receiving treatment for cancer</b>		
<p>Cancer treatment is associated with serious side-effects, including disruption in the function and integrity of the mouth. These complications (e.g. mucositis, oral candidiasis) may cause pain, poor nutrition, delays in cancer treatment, increased hospital stays and costs and, in some patients, life-threatening septicaemia.</p> <p>Our underpinning research comprises five Cochrane reviews, focusing on prevention and treatment of debilitating oral conditions in patients receiving cancer treatment.</p>		

We evaluated benefits and harms of interventions to manage mucositis/candidiasis. Key findings were:

- High certainty evidence from a large number of trials (4,226 participants) indicated that drugs absorbed or partially absorbed from the gastrointestinal tract prevent oral candidiasis when compared with no treatment or with drugs not absorbed from the gastrointestinal tract [1].
- Several interventions were found to be beneficial for preventing or reducing the severity of mucositis associated with cancer treatment. Specific treatments may be more beneficial for those with certain cancers, receiving certain treatment [2]. This conclusion was based on data from 131 studies with 10,314 participants. Two published updates to this review using hitherto unpublished data were conducted, looking specifically at the use of oral cryotherapy (cooling of the mouth), cytokines and growth factors [3, 4].
  - Oral cryotherapy was found to lead to large reductions in oral mucositis of all severities in adults receiving fluorouracil (5FU), a common chemotherapy treatment for solid cancers [3].
  - Keratinocyte growth factor appears to be a relatively safe and effective intervention, which is likely to reduce the risk of oral mucositis in adults who are receiving either radiotherapy to the head and neck with chemotherapy, or chemotherapy alone for mixed solid and blood cancers [5].

### Prevention of VAP in critically ill patients receiving mechanical ventilation

VAP is defined as pneumonia that develops in critically ill patients who have received mechanical ventilation for at least 48 hours. It is the most frequent infection occurring in patients after admission to the intensive care unit (ICU). It is estimated that more than 300,000 patients receive mechanical ventilation in the US each year.

We produced a large, seminal review focused on the use of oral care measures to reduce morbidity and mortality from VAP in critically ill patients (identified as a priority topic in a 2014 international prioritisation exercise).

The VAP review [6] analysed evidence from 38 randomised controlled trials including 6,016 participants and concluded:

- There is high certainty evidence that chlorhexidine mouth rinse or gel reduces the risk of VAP compared to placebo or usual care from 24% to about 18%. For every 17 ventilated patients in intensive care receiving oral hygiene care that includes chlorhexidine, one outcome of VAP will be prevented [6].

### 3. References to the research

Cochrane Reviews, as produced by COH at UoM, are systematic reviews of primary research in human health care and health policy and are internationally recognised as the highest standard in evidence-based health care. Accurate, concise and unbiased synthesis of the available evidence are invaluable in informing decision-makers.

1. **Clarkson JE, Worthington HV**, Eden TOB. Interventions for preventing oral candidiasis for patients with cancer receiving treatment. *Cochrane Database Systematic Reviews* 2007, Issue 1. Art. No.: CD003807. doi: [10.1002/14651858.CD003807.pub3](https://doi.org/10.1002/14651858.CD003807.pub3) (19 citations, Web of Science (WoS), 12 January 2021).
2. **Worthington HV, Clarkson JE**, Bryan G, Furness S, **Glenny AM**, Littlewood A, **McCabe MG**, Meyer S, Khalid T. Interventions for preventing oral mucositis for patients with cancer receiving treatment. *Cochrane Database of Systematic Reviews* 2011, Issue 4. Art. No.: CD000978. doi: [10.1002/14651858.CD000978.pub5](https://doi.org/10.1002/14651858.CD000978.pub5) (143 citations, WoS, 12 January 2021).
3. **Riley P, Glenny AM, Worthington HV**, Littlewood A, **Clarkson JE, McCabe**

**MG.** Interventions for preventing oral mucositis in patients with cancer receiving treatment: oral cryotherapy. *Cochrane Database of Systematic Reviews* 2015, Issue 12. Art. No.: CD011552. doi: [10.1002/14651858.CD011552.pub2](https://doi.org/10.1002/14651858.CD011552.pub2) (46 citations, WoS, 12 January 2021).

4. **Riley P, Glenny AM, Worthington HV,** Littlewood A, Fernandez Mauleffinch LM, **Clarkson JE, McCabe MG.** Interventions for preventing oral mucositis in patients with cancer receiving treatment: cytokines and growth factors. *Cochrane Database of Systematic Reviews* 2017, Issue 11. Art. No.: CD011990. doi: [10.1002/14651858.CD011990.pub2](https://doi.org/10.1002/14651858.CD011990.pub2) (10 citations, WoS, 12 January 2021).
5. **Clarkson JE, Worthington HV,** Furness S, **McCabe M,** Khalid T, Meyer S. Interventions for treating oral mucositis for patients with cancer receiving treatment. *Cochrane Database of Systematic Reviews* 2010, Issue 8. Art. No.: CD001973. doi: [10.1002/14651858.CD001973.pub4](https://doi.org/10.1002/14651858.CD001973.pub4) (66 citations, WoS, 12 January 2021).
6. Hua F, Xie H, **Worthington HV,** Furness S, Zhang Q, Li C. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database of Systematic Reviews* 2016, Issue 10. Art. No.: CD008367. doi: [10.1002/14651858.CD008367.pub3](https://doi.org/10.1002/14651858.CD008367.pub3) (92 citations, WoS, 12 January 2021).

#### 4. Details of the impact

##### Context

It is recognised that good oral health is important in supporting general health. Our research focused on the care of medically compromised patients.

Before our research there was an absence of robust synthesised evidence of large, complex bodies of evidence. Existing reviews were of low quality and/or restricted to particular subsets of interventions or cancer types, resulting in sub-optimal recommendations being promoted.

##### Pathways to impact

Our research focused on providing robust evaluations of the comparative effectiveness of different measures to promote health via oral hygiene. These findings are included in multiple national and international clinical guidelines informing recommendations that are key to the planning and provision of oral health care world-wide.

##### Reach and significance of the impact

###### Prevention and treatment of oral conditions in patients receiving treatment for cancer

Our research has been used to inform several major guidelines, underpinning recommendations, reducing the advocacy of ineffective interventions (e.g. nystatin and chlorhexidine) and improving health outcomes in medically compromised patients. The impact of our research is illustrated by the number, scope and reputation of the guidelines our work has informed. For example:

- UK NICE Clinical Knowledge Summary Palliative Care makes recommendations for those receiving chemotherapy and radiotherapy based entirely on our research findings (2018) [A].
- Mucositis Prevention Guideline Development Group makes international recommendations for the prevention of oral and oropharyngeal mucositis in children receiving treatment for cancer (2015) [B].
- Association of the Scientific Medical Societies in Germany presents guidelines for supportive therapy for oncological patients (2016) [C].

Alongside the clinical implications of preventing oral complications of cancer treatment, there are also significant financial implications associated with mouth care management. One

recent publication found that the incremental cost of managing oral mucositis was approximately USD5,000 to USD30,000 among patients receiving radiation therapy and USD3,700 per cycle among patients receiving chemotherapy (Elting LS, Chang YC. Costs of Oral Complications of Cancer Therapies: Estimates and a Blueprint for Future Study. J Natl Cancer Inst Monogr. 2019 Aug 1;2019(53):lgz010. doi: 10.1093/jncimonographs/lgz010).

Our research is being used to directly inform patients about aspects of their clinical care including: Lymphoma action [Di] and Oncolink patient information on side-effects of treatment [Dii].

#### Prevention of VAP in critically ill patients receiving mechanical ventilation

Again, our research underpins international Guidelines, including:

- Valvular Disease Working Group of the French Society of Cardiology, Society of Oral Surgery, Society of Periodontology and Oral Implantology, Society of Endodontics and Society of Infectious Pathology provide recommendations on management of oral status in patients with valvular disease (2017) [E].
- Korean Nursing Practice Guidelines for Oral Care provide national evidence-based guidelines for clinical nursing care settings (2020) [F].

Further integration of our research has been supported by NHS Improvement Saving Lives guidance, supporting healthcare providers to reduce healthcare-associated infections and variation in care (2017) [G]. Our review is the single systematic review source supporting oral hygiene measures as a high impact intervention in the reduction of VAP. Inclusion of oral care as one of six core elements of the care process enhances the impact of evidence in this area. Quality improvement studies showed that implementing a VAP care bundle, with an evidence-based oral hygiene component, resulted in a significant, sustained improvement in resident oral health (2018) [H]. It also significantly reduced the incidence rate of VAP (a reduction of 21% in days intubated), duration of invasive ventilation (12.8 to 12.4 days), ICU length of stay (3 days) and mortality rate (8%) (2019) [I].

There has been further impact on practice through the integration of evidence into practitioner educational material. NHS Health Education England have developed teaching aids that seek to address shortcomings in oral care often observed in hospital and community care. Our research provides the evidence-base for oral care measures for ventilated patients. Subsequently, a Mouthcare Matters MOOC has used our research to inform their training. The author states: "*Alongside clinical expertise, evidence from the Cochrane reviews has been key to informing the development of MCM educational materials for reducing the incidence of ventilator-associated pneumonia and for preventing and treating mucositis in people being treated for cancer.*" [J].

#### **5. Sources to corroborate the impact**

- A. National Institute for Health and Care Excellence. Clinical Knowledge Summaries: Palliative care - oral (last revised October 2018). London: National Institute for Health and Care Excellence; 2018 October. Available from: <http://cks.nice.org.uk/palliative-care-oral>  
*NICE recommendations for oral-palliative-care based solely on COH mucositis and candidiasis reviews.*
- B. Sung L, Robinson P, Treister N, Baggott T, Gibson P, Tissing W, Wiernikowski J, Brinklow J, Dupuis LL.; The Mucositis Prevention Guideline Development Group. Guideline for the prevention of oral and oropharyngeal mucositis in children receiving treatment for cancer or undergoing haematopoietic stem cell transplantation. BMJ Support Palliat Care. 2015 Mar;7(1):7-16. doi: [10.1136/bmjspcare-2014-000804](https://doi.org/10.1136/bmjspcare-2014-000804)  
*Guidelines informed by COH mucositis reviews, developed by interdisciplinary, international team of experts.*
- C. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe,

AWMF). S3-Leitlinie Supportive Therapie bei onkologischen PatientInnen. (S3 guideline: Supportive therapy for oncological patients). Berlin: Deutsche Krebsgesellschaft (DKG); 2016. Available from: <http://www.awmf.org/leitlinien/detail/II/032-054OL.html>

*Evidence based guidelines developed by Association of the Scientific Medical Societies in Germany, using COH mucositis reviews as underpinning evidence.*

- D. Patient information websites highlighting best practice mouthcare for cancer patients:

Di. Lymphoma Action: <https://lymphoma-action.org.uk/about-lymphoma-side-effects-treatment/sore-mouth-oral-mucositis>

Dii. Oncolink: <https://www.oncolink.org/support/side-effects/gastrointestinal-side-effects/mucositis/all-about-mucositis>

- E. Millot, S., et al, 2017. Position paper for the evaluation and management of oral status in patients with valvular disease: Groupe de Travail Valvulopathies. Archives of Cardiovascular Diseases 110, 482–494. doi:[10.1016/j.acvd.2017.01.012](https://doi.org/10.1016/j.acvd.2017.01.012)

*Current evidence from COH has led the working group to suggest the use of 0.12% or 0.2% chlorhexidine mouthwash 1 day systematically before valvular intervention.*

- F. Cho, Y. A. et al. (2020) Updates of Nursing Practice Guideline for Oral Care. Journal of Korean Clinical Nursing Research, 26(2), pp. 141–153. doi: [10.22650/JKCN.2020.26.2.141](https://doi.org/10.22650/JKCN.2020.26.2.141) (Abstract in English, article in Korean).

*Korean guidelines underpinned by COH review on VAP.*

- G. Infection Prevention Society and NHS Improvement. 4th edition, April 2017. Saving Lives: High Impact Interventions, Care processes to prevent infection.

*COH VAP review is the only systematic review to be included in these guidelines for oral hygiene measures for high impact interventions to prevent ventilator-associated pneumonia.*

- H. Finch Guthrie, Patricia; Rayborn, Shelley; Boatright, John; Pearson, Valinda; Wieting, Rosemary; Peterson, Randy; Danahy, Molly. Improving Resident Oral Health and Adherence to a Ventilator-Associated Pneumonia Bundle in a Skilled Nursing Facility, Journal of Nursing Care Quality: October/December 2018 - Volume 33 (4), p 316-325 doi: [10.1097/NCQ.0000000000000321](https://doi.org/10.1097/NCQ.0000000000000321)

*Shows a significant improvement in oral health (a mediating variable for pneumonia) based on a care bundle incorporating oral hygiene measures based on COH VAP review.*

- I. Sousa AS, Ferrito C, Paiva JA. Application of a ventilator associated pneumonia prevention guideline and outcomes: A quasi-experimental study. Intensive Crit Care Nurs. 2019;51:50-56. doi:[10.1016/j.iccn.2018.10.001](https://doi.org/10.1016/j.iccn.2018.10.001)

*Shows a significant reduction in incidence of VAP, duration of invasive ventilation, ICU stay and mortality based on a care bundle incorporating oral hygiene measures based on COH VAP review.*

- J. Supporting letter from 2020 from Mouth Care Matters Consultant Lead and author of Mouth Care Matters MOOC.

*MOOC builds on Health Education England education material to address shortcomings in oral care often observed in hospital and community care (Mouth Care Matters <https://mouthcarematters.hee.nhs.uk>).*